A Single-Center, Randomized, Investigator/Subject-Blind, Adaptive Single Ascending-Dose, Placebo-Controlled, Parallel Study to Investigate the Safety, Tolerability, Pharmacokinetics (Including the Effect of Food), and Pharmacodynamics of RO5545965 Following Oral Administration in Healthy Subjects.

Published: 25-09-2012
Last updated: 26-04-2024

to assess the safety and tolerability of single ascending doses of RO5545965 in healthy subjectsto investigate the pharmacokinetics (PK) of RO5545965 (and its metabolite(s) if appropriate)to investigate the pharmacodynamic (PD) effects of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON36943

Source
ToetsingOnline

Brief title
RO5545965 SAD and FE study

Condition

- Schizophrenia and other psychotic disorders

Synonym
psychiatric disorders, Schizofrenia

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Psychosis, RO5545965, Schizofrenia, Single dose

Outcome measures

Primary outcome

Pharmacodynamics: Prolactin

Pharmacokinetics: plasma/urine drug concentrations

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination, ESRS-A, DSST, Bond & Lader VAS

Secondary outcome

NA

Study description

Background summary

RO5545965 is a new investigational compound that may eventually be used for the treatment of psychosis and schizophrenia. RO5545965 is not registered as a drug. This is the first time that this compound is being given to humans. RO5545965 will be administered in form of a capsule.

Study objective

to assess the safety and tolerability of single ascending doses of RO5545965 in healthy subjects
to investigate the pharmacokinetics (PK) of RO5545965 (and its metabolite(s) if appropriate)
to investigate the pharmacodynamic (PD) effects of RO5545965
to assess the effect of food on the PK of a single dose of RO5545965

Study design

Procedures and assessments
Screening and follow-up:
clinical laboratory, physical examination,12-lead ECG, vital signs; at eligibility screening: medical history, drug- and alcohol screen, HBsAg, anti HCV, anti-HIV 1/2

Observation period:
each period in clinic from -42h (Day -2) up to 48h (Day 3) after drug administration (Day 1) with an ambulatory visit on Day 5

Blood sampling:
For pharmacokinetics: Day 1 pre-dose and at 30 minutes and 1, 1.5, 1.75, 2, 2,5 , 3, 4, 5, 6, 8, 10, 12, 24 and 48 hours post-dose;
For pharmacodynamics (prolactine measurements): pre-dose on Day 1 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8 and 10 hours post-dose and time-matched on Day -1
For genotyping; on Day 1 (mandatory)

Urine sampling:
For pharmacokinetics: Day 1 pre-dose and at intervals 0-4h, 4-12h, 12-24h and 24-48h

Safety assessments:
Adverse events throughout the study. Clinical laboratory, hematology, urinalysis, coagulation (screening only), physical examination, vital signs, 12-lead-ECG and weight at screening and follow-up

Special safety assessments:
Bond & Lader VAS, DSST (Digit Symbol Substitution Test), ESRS - A (Extrapyramidal Symptom Rating Scale - Abbreviated)

Intervention

Part 1: subjects will receive a single dose of RO5545965 as an oral capsule
Part 2: subjects will receive a single dose per period of RO5545965 as an oral

capsule

Study burden and risks

Registration of adverse effects: During the entire investigation all adverse effect will be documented.

Blood draw (for pharmacokinetics & pharmacodynamics and lab safety tests), indwelling canula: During this study blood will be drawn. It is anticipated that an indwelling canula will be used and blood draws will be drawn by direct puncture of the vein.

Collection of urine: Urine will be collected until 48 hours after administration of RO5545965 or placebo.

Heart trace (ECGs): ECGs will be made regularly.

Blood pressure and pulse rate (vital signs): Vital signs will be measured regularly.

Blood sample for DNA tests: On Day 1 a blood sample will be taken for possible DNA tests. Participation in this part of the study is mandatory.

Bond & Lader VAS: This Visual Analogue Scale will be used to assess alertness, calmness and contentment.

DSST: This digit symbol substitution test, consisting of a combination of symbols and numbers will test the mental status

ESRS-A: A physician will examine on Days -1, 1 and 3 using the Extrapyramidal Symptoms Rating Scale - Abbreviated; a combination of a clinical interview, as well as motor examination to test the physical status.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy male subjects
18-45 yrs, inclusive
BMI 18 to 30 kg/m2, inclusive
Light smokers or non-smokers

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS.
Participation in another drug study within 90 days before screening, as calculated from the day of follow-up from the previous study.
Any donation of blood or significant blood loss within 3 months prior to first administration of the study drug.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2012
Enrollment:	92
Type:	Actual

Ethics review

Approved WMO Date:	25-09-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-10-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-002869-35-NL
CCMO	NL42082.056.12